PHC CH 11: HIV and AIDS
AHL CH 10: HIV and AIDS

National Department of Health

Affordable Medicines Directorate
Essential Drugs Programme

Primary Healthcare Level Standard Treatment Guidelines – 2020-4 Review cycle
Adult Hospital Level Standard Treatment Guidelines – 2020-4 Review cycle

Evidence

Please access the National Essential Medicines List Committee (NEMLC) report for detailed evidence (including rationale, references and costings) informing decision-making on medicine addition, amendments and deletions:

NHI Website: https://www.health.gov.za/nhi-edp-stgs-eml
Knowledge Hub: www.knowledgehub.health.gov.za/e-library

Disclaimer

This presentation is an implementation tool and should be used alongside the most recently published STGs available on the Knowledge Hub. This information does not supersede or replace the STGs.

****NB This webinar presentation covers Adults and Adolescents ONLY!! Please refer to the Paediatric Hospital Level STG HIV Chapter for updates pertaining to children.**

https://www.health.gov.za/wp-content/uploads/2024/02/Paediatric-Chapter-9_HIV-chapter_2023_updatedNovember2023.pdf

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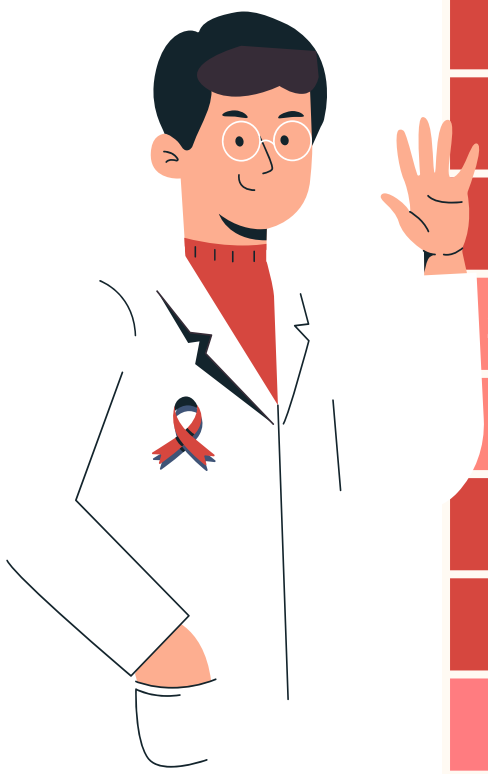
South Africa 1994 - 2024

Presentation Outline



- Summary of ART Regimens
- Dolutegravir in Pregnancy
- 2nd Line Antiretroviral Therapy Regimens: Recycling TDF
- 2nd Line Antiretroviral Therapy Regimens: Atazanavir/ritonavir
- Tuberculosis Preventative Therapy (TPT)
- Pre-exposure Prophylaxis (PrEP)
- Monitoring on ART: Cryptococcal Antigen (CrAg) Screening
- Cryptococcosis
- Post-Exposure Prophylaxis: Notable Amendments

Summary of ART Regimens

Initiating ART

Treatment Naïve Patients

Individuals ≥30kg and ≥10 years

TDF + 3TC + DTG

DTG-based regimens are now recommended as first line ART in all women of childbearing potential.

Patients on rifampicin-based TB treatment

TDF + FTC + EFV

OR

TDF + 3TC + DTG **+** **DTG** (additional dose 50mg, 12 hours later)

The extra DTG dose can be stopped two weeks after stopping rifampicin.

Contraindications/ Intolerance to DTG

TDF + 3TC/FTC + EFV

Summary of ART Regimens

Contraindications to EFV and DTG

Start protease inhibitor-based regimen

TDF + 3TC/FTC + ATV/r

if patient requires rifampicin-based TB treatment, substitute ATV/r with LPV/r at 800/200 mg 12-hourly.

Note: There is an increased risk of ALT/AST elevations and gastrointestinal disorders. LPV/r dose should be gradually titrated upward over 1-2 weeks (e.g. 600/150 mg and then 800/200 mg).

The LPV/r can be switched back to ATV/r two weeks after completion of TB therapy

Contraindication to TDF
» eGFR <50ml/minute

If chronic hepatitis B coinfection and eGFR 30-50 ml/min

TAF + FTC + DTG

Other scenarios:

ABC + 3TC + DTG

****TDF to be added at an interval adjusted for the degree of renal dysfunction**

Summary of ART Regimens

Contraindication to TDF/TAF and ABC intolerance/hypersensitivity	AZT + 3TC + DTG

Note: In the unlikely scenario where there is intolerance/contraindication to all currently available NRTIs, the following alternative dual-therapy regimens may be used after consulting a specialist:

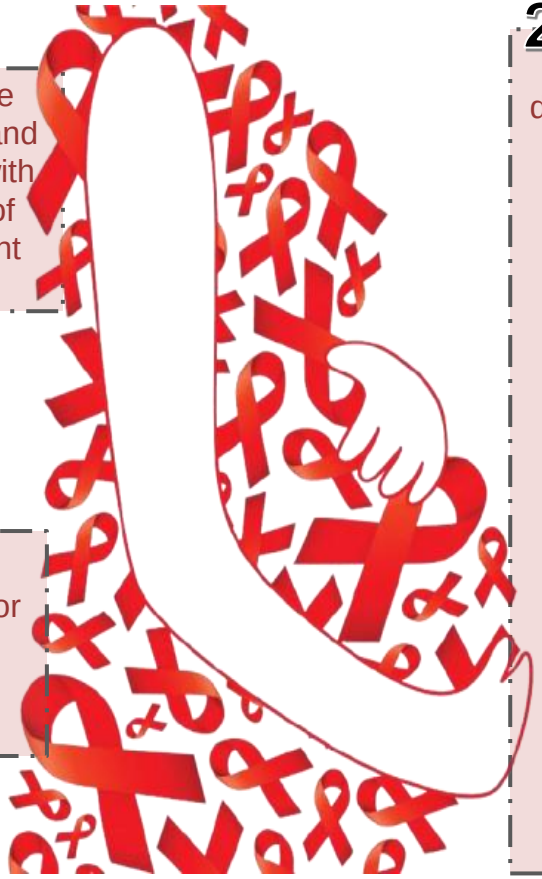
- DTG + 3TC (if no resistance/intolerance to 3TC and VL < 500 000 copies /mL)
- EFV + LPV/r
- DTG + LPV/r

Dolutegravir in Pregnancy

Medicine Review: Dolutegravir (DTG) in Pregnant Women and Women of Child-Bearing Potential (WOCP)

1

This review, which is a second update of the 2017 review, considered evidence of safety and efficacy of DTG containing ART, compared with efavirenz (EFV) containing ART in women of child-bearing potential (WOCP) and pregnant women.



2

The estimate of prevalence of neural tube defects (NTDs) in infants born to women on (DTG) has declined since the original safety signal from the Botswana Tsepamo study as more data in that cohort has accrued. The current estimate is approximately 2 NTDs per 1000 births.

- In the July 2020 update from this study there were 7 NTDs in 3591 births with DTG exposure (0.19%; 95%CI 0.09% to 0.40%), and 8 NTDs in 10,958 births with EFV exposure from conception (0.07%; 95%CI 0.03% to 0.17%).
- There was no significant difference in NTD prevalence between DTG and EFV at conception (difference 0.12%; 95%CI -0.001% to 0.33%).
- In HIV-uninfected women there were 87/119,630 with NTD (0.07%; 95%CI 0.06, 0.09%)

3

The Dolphin 2 study, randomised pregnant women of 28 or more weeks to DTG (n=129) or EFV (n=128)

- HIV viral load < 50 copies/mL at delivery: DTG 74.2% vs EFV 42.7%

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National Department of Health: Affordable Medicines, EDP-Primary Healthcare/Adult Hospital level. Medicine Review: Dolutegravir in Pregnant Women and Women of Child-Bearing June 2021. http://www.health.gov.za/. DTG-in-pregnancy_PHC-Adults-Medicine-review_17June2021_v2.pdf (health.gov.za)

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Dolutegravir in Pregnancy

Medicine Review: Dolutegravir in Pregnant Women and Women of Child-Bearing Potential (WOCP)

4

A multicentre trial, including 643 pregnant women at 14-28 weeks gestation, randomised women to DTG/FTC/TAF (n=217), DTG/FTC/TDF (n=215) or EFV/FTC/ TDF (n=211).

- At delivery, more participants were virally suppressed in the combined DTG containing groups than the EFV group, 98% vs 91%, difference 6·5% (95% CI 2.0% to 10.7).
- Neonatal mortality was highest in the EFV group: DTG/FTC/TAF group 1% vs DTG/FTC/TDF 2% vs EFV 5%.
- Composite adverse pregnancy outcome (preterm delivery/ small for gestational age/stillbirth/ spontaneous abortion) was lower in the DTG/FTC/TAF group: DTG/FTC/TAF group 24% vs DTG/3TC/TDF 33% vs EFV 33%
- Preterm deliveries were most common in the EFV group: DTG/FTC/TAF 6% vs DTG/3TC/TDF 9% vs EFV 12%.
- Mean weight gain was highest in the DTG/FTC/TAF group: DTG/FTC/TAF 0.378kg/week vs DTG/FTC/TDF 0.319 kg/week vs EFV/FTC/TDF 0.291kg/week. Mean weight gain in all 4 groups was lower than that recommended by the Institute of Medicine during the 2nd and 3rd trimester.

5

In a RCT comparing TAF/FTC/DTG, TDF/FTC/DTG and TDF/FTC/EFV, 10% of women were obese at baseline. At 48 weeks 20% of women on TAF/FTC/DTG , 11% on TDF/FTC/DTG 9% on TDF/FTC/EFV had new onset obesity.

6

In an observational cohort study in Botswana including data from 1235 HIV exposed infants whose mothers took DTG/TDF/FTC in pregnancy, and 2411 whose mothers took EFV/TDF/FTC, mother to child transmission (MTCT) was rare when either regimen started before conception: DTG 0/213 (0%, 95% CI 0.00% to 1.72%) vs EFV 1/1497 (0.07%, 95% CI 0.00% to 0.37%). MTCT rates were similar when ART was started during pregnancy DTG 8/999 vs EFV 8/883 Risk difference 0.11% (95% CI -0.79 to 1.06%).

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Dolutegravir in Pregnancy

Rationale for recommendation

1. The estimated risk of neural tube defects in infants exposed to DTG in early pregnancy that was first identified in the Tsepamo observational study in Botswana has diminished over time, with the accumulation of further data. The risk difference between DTG and efavirenz is no longer significant.

2. DTG (especially when combined with tenofovir alafenamide) is associated with more weight gain during pregnancy than efavirenz, but the difference is of uncertain clinical relevance.

3. A standardised regimen for all adults and adolescents living with HIV is likely to be easier to provide.

4. DTG causes more rapid viral suppression than efavirenz, resulting in increased viral suppression rates by time of delivery in randomised controlled trials of ART initiation in the second and third trimester of pregnancy. This has not yet translated into a demonstrable difference in mother-to-child transmission risk, but event rates are very low with both regimens.

5. Based on those findings and observations, the PHC/Adult Hospital Level Committee feel that the potential long-term benefits to pregnant women and WOCP (Women of Child Bearing Potential), as well as potential short-term benefits to their infants, outweigh the risks

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Dolutegravir in Pregnancy

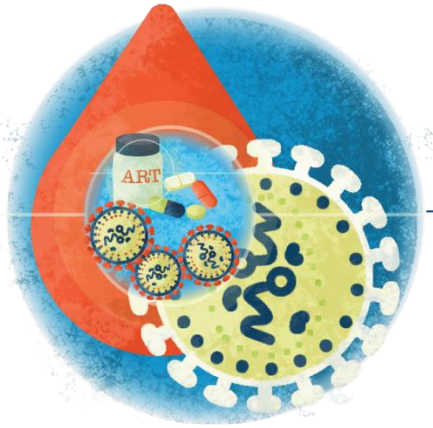
NEMLC Recommendation

NEMLC recommends that dolutegravir should be part of the preferred first line ART regimen for all adults and adolescents living with HIV, including pregnant women and women of child-bearing potential. The existing contra-indication in pregnancy should be removed from the STG ***(strong recommendation).***

This supports the universal test-and-treat (UTT) strategy of the National HIV Programme. It was also duly noted that the South African Health Products Regulatory Authority are currently reviewing the label of dolutegravir products registered on the South African market.

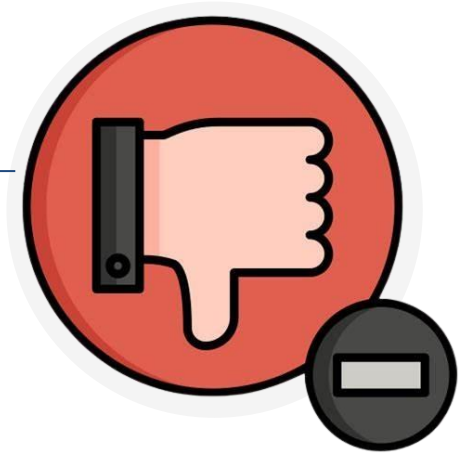
2ND Line Antiretroviral Therapy Regimens: Recycling TDF

Background



According to current Department of Health and World Health Organization guidelines, if patients fail a first-line tenofovir (TDF)-based first line regimen, TDF should be switched to zidovudine (AZT) as part of 2nd -line combined antiretroviral therapy.

This is to prevent there being only one fully active drug in the new regimen. (The other nucleoside reverse transcriptase inhibitor (NRTI) in the regimen, interchangeably either lamivudine or emtricitabine, is typically reused in 2nd line therapy as it is well-tolerated, retains significant antiviral activity even in the face of the signature M184V mutation, and viruses harbouring the M184V mutation are hyper-susceptible to AZT.)



However, using AZT has several disadvantages: it is poorly tolerated, it needs to be given twice daily, it requires more frequent monitoring, and it is more expensive. Observational data has to date suggested that the switch to AZT might not be necessary

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National Department of Health: Affordable Medicines, EDP-Primary Healthcare/Adult Hospital level. Evidence Summary: Recycling tenofovir in 2nd line antiretroviral therapy: evidence from NADIA and ARTIST Trials, May 2022. http://www.health.gov.za/. TDF-backbone-as-2nd-line-in-HIV_Adults_Evidence-summary_19May2022_-v3.0.pdf (health.gov.za)

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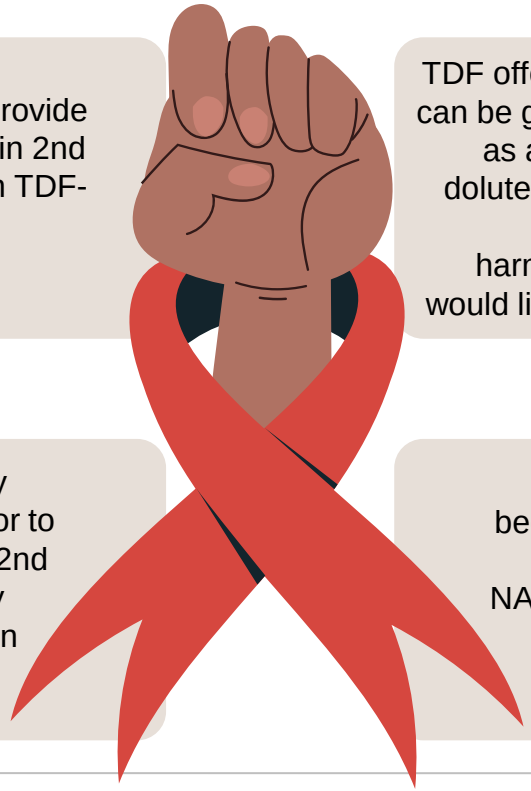
2ND Line Antiretroviral Therapy Regimens: Recycling TDF

RESULTS SUMMARY:

The NADIA, ARTIST and VISEND trials provide evidence that TDF may safely be reused in 2nd -line therapy following 1st -line failure with TDF-containing regimens.

TDF offers substantial additional benefits over AZT: it can be given once daily (vs twice daily), it is available as a fixed-dose combination with lamivudine and dolutegravir (i.e. TLD), it requires less intense initial monitoring, it is cheaper, and the greater harmonisation with first line TDF-based regimens would likely improve 2nd -line drug stock challenges.



Together, the trials offer moderate quality evidence that recycled TDF is non-inferior to AZT with respect to viral suppression in 2nd line antiretroviral therapy, and low quality evidence that it may be superior to AZT in suppression.

TDF's signature K65R mutation, which has been associated with reduced HIV viral fitness, is a key driver of these results, and thus the NADIA and ARTIST data cannot necessarily be extrapolated to support the reuse of other NRTIs such as ABC or AZT.

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2ND Line Antiretroviral Therapy Regimens: Recycling TDF

NEMLC Recommendation

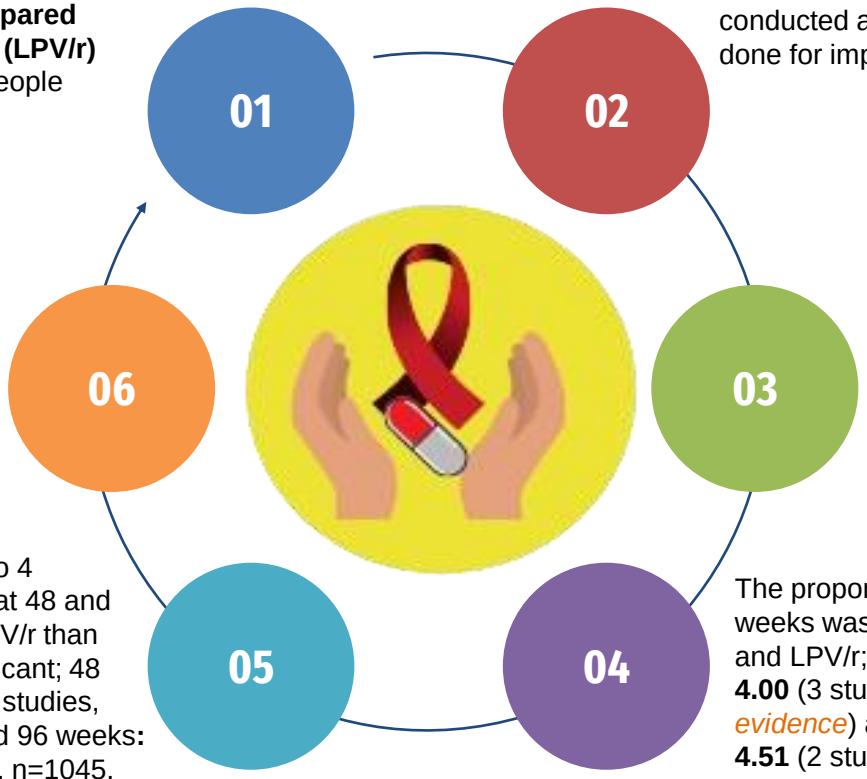
NEMLC recommends that tenofovir should be recycled in 2nd line dolutegravir-based antiretroviral therapy.

2ND Line Antiretroviral Therapy Regimens: Atazanavir/ritonavir

Medicine Review: ATAZANAVIR/RITONAVIR vs LOPINAVIR/RITONAVIR for Adult HIV Patients

A **review** was conducted of **ritonavir-boosted atazanavir (ATV/r) compared with ritonavir-boosted lopinavir (LPV/r)** in protease inhibitor naïve adult people living with HIV (PLHIV).

3 randomised controlled trials were conducted and **meta-analyses** was done for important clinical outcomes.



The proportion of patients with **treatment discontinuations due to AEs** at 48 and 96 weeks was numerically lower with ATV/r than LPV/r, but this was not statistically significant; 48 weeks: **RR 0.65, 95%CI 0.37 to 1.15** (3 studies, n=1104, *moderate certainty evidence*) and 96 weeks: **RR 0.54, 95%CI 0.29 to 1.00** (2 studies, n=1045, *moderate certainty evidence*).

The proportion of patients **with viral load <50 copies/mL** at 48 and 96 weeks was slightly higher (about 10%) with ATV/r than LPV/r; 48 weeks: **relative risk (RR) 1.11, 95% confidence interval (CI) 1.04 to 1.18** (3 studies, n=1105, *moderate certainty evidence*) and 96 weeks: **RR 1.09, 95%CI 1.01 to 1.19** (2 studies, n=1045, *moderate certainty evidence*).

The proportion of patients with grade 2 to 4 treatment related **adverse events (AE)** at 48 and 96 weeks was numerically lower with ATV/r than LPV/r, but this was not statistically significant; 48 weeks: **RR 0.88, 95% CI 0.73 to 1.06** (3 studies, n=937, *moderate certainty evidence*) and 96 weeks**: RR 0.88, 95% CI 0.73 to 1.06** (2 studies, n=1045, *moderate certainty evidence)*

The proportion of **patients who died** by 48 and 96 weeks was not significantly different between ATV/r and LPV/r; **48 weeks: RR 1.01, 95% CI 0.25 to 4.00** (3 studies, n=942, *moderate certainty evidence*) and **96 weeks: RR 1.55, 95% CI 0.53 to 4.51** (2 studies, n=1045, *moderate certainty evidence*)

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National Department of Health: Affordable Medicines, EDP-Primary Healthcare/Adult Hospital level. Medicine Review: Atazanavir/Ritonavir vs Lopinavir/Ritonavir for Adult HIV Patients, November 2021. http://www.health.gov.za/. Atazanavir-ritonavir-vs-lopinavir-ritonavir-as-2nd-line-adult-HIV-therapy_18-November-2021_Final.pdf (health.gov.za)

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2ND Line Antiretroviral Therapy Regimens: Atazanavir/ritonavir

NEMLC Recommendation

NEMLC suggests ritonavir-boosted atazanavir be the preferred protease inhibitor for second-line therapy in all adult patients without concomitant TB. Ritonavir-boosted lopinavir must still be available for use with rifampicin-containing TB therapy (conditional recommendation). It was furthermore noted that the global market is shifting from LPV/r to other protease inhibitors (i.e., DRV/r and ATV/r) and competition will likely push down the price of other protease inhibitors.

Rationale: Ritonavir-boosted atazanavir is at least non-inferior to ritonavir-boosted lopinavir in terms of viral suppression, is associated with fewer gastrointestinal side-effects and lipid profile abnormalities than ritonavir-boosted lopinavir and is dosed once-daily.

Tuberculosis Preventative Therapy (TPT)

Background

During the previous review cycles, the NEMLC approved 12 months of daily isoniazid (12H) for PLHIV and not Rifapentine + Isoniazid (3HP)

Non-inferiority trials suggested that 3HP prophylaxis was not inferior to 12H in PLHIV. However, 3HP is more expensive than 12H.

Current 2020-3 review cycle: In the current review cycle, 3HP was recommended for inclusion to the therapeutic interchange database:

- **12H:** Isoniazid, oral, 300 mg daily for 12 months
- **3HP:** Isoniazid, oral 900 mg + Rifapentine, oral 900 mg weekly for 3 months (preferably as an FDC).

Tuberculosis Preventative Therapy (TPT)

NEMLC Recommendation

NEMLC recommends that 3HP be included as a therapeutic alternative to 12H in PLHIV initiated on ART – however, for DTG-containing regimens patients to be virally suppressed (this would promote competitive pricing).

However, as there is currently no available RCT evidence for concomitant use of rifapentine with viraemic patients on DTG, the following text was added to the STG:

Adults and adolescents initiating a DTG-containing ART regimen:

- Isoniazid daily for 12 months is the preferred regimen.

For patients who are already virally suppressed on a DTG-based regimen:

- A weekly combination of isoniazid (900mg if weight >30 kg) plus rifapentine (900mg if weight >30 kg) for three months may be used.
  - Do not use rifapentine-containing TPT in patients on protease inhibitor-based ART, or in women on hormonal contraceptives. [*See the therapeutic interchange database for details regarding the rifapentine-containing TPT regimen*].
  - Educate patients on the symptoms of hepatotoxicity (nausea, vomiting, yellow eyes, brown urine, and pain in right upper quadrant) associated with TPT.

ADD

- Pyridoxine, oral, 25 mg once daily for the full duration of the TPT regimen.
  - Instruct patient to present early if any of these symptoms arise.
  - Follow patients up monthly for the first 3 months.

The therapeutic interchange database update as follows:

Indication	Criteria	Medicine (INN)	Treatment course	Therapeutic class	Therapeutic ATC
TPT for ART-naïve HIV adult patients	n/a	Isoniazid	300 mg daily x 12 months	TPT	J04A
	• Initiated on TEE • Initiated on TLD BUT virally suppressed • NOT on a PI • Not on oral hormonal contraceptives	Isoniazid and rifapentine (FDC)	900/900 mg weekly x 3 months	TPT	J04A

FDC=fixed dose combination; TEE= TDF+EFV+FTC; TLD= TDF+3TC+DTG; TPT=TB preventive therapy; PI=protease inhibitor

Pre-Exposure Prophylaxis (PrEP)

What are the current PrEP options available on the EML?

Oral Fixed Dose Combination:
TDF (300mg) + FTC (200mg)

Which PrEP options are non-EML and why?

Dapivirine Vaginal Ring

NEMLC Recommendation: NEMLC suggests not to use the dapivirine ring as an additional option for prevention of HIV acquisition in women (conditional recommendation).

Rationale:

- Available evidence for the dapivirine ring is restricted to placebo-controlled data, with no studies comparing dapivirine to oral tenofovir plus emtricitabine, the current standard of care in South Africa.
- There is currently no data for efficacy in adolescents.
- The dapivirine ring cannot be used in pregnancy.
- There is a sub-group of women who cannot use tenofovir plus emtricitabine for whom the dapivirine ring may be an option.
- However, at the current proposed price, dapivirine is unaffordable. The estimated threshold price for reviewing this recommendation is R52.00 per ring

https://www.health.gov.za/wp-content/uploads/2024/03/DapivirineRingForPrEP_PHC-Review_9June2022_v5.pdf

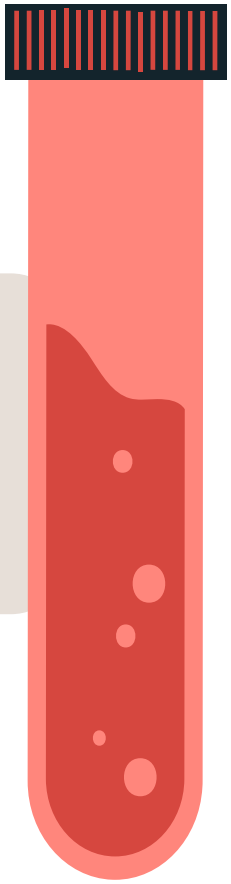
Cabotegravir Long-Acting Injection

NEMLC Recommendation: Although the efficacy of CAB is high, and the safety profile acceptable, the NEMLC suggests not to use CAB as PrEP for HIV, until such time as the price becomes known, and the evidence of efficacy for regimens that do not include an oral lead-in phase are available.

Rationale:
Two phase 3 RCTs both found that PrEP with long-acting injectable CAB had greater efficacy than oral tenofovir plus emtricitabine. A model to assess budgetary impact and cost-effectiveness analysis has been developed, however until a price is confirmed, a final recommendation cannot be made.

https://www.health.gov.za/wp-content/uploads/2024/03/Cabotegravir-as-PrEP-for-adults-_EvidenceSummary_15May2022-v3.pdf

Monitoring on ART: Cryptococcal Antigen (CrAg) Screening



CrAg Screening

Reflex screening of Cryptococcal Antigen (CrAg) in PLHIV was amended to CD4<200 cells/mm[3]

Current WHO guidelines states: “Screening for cryptococcal antigen followed by pre-emptive antifungal therapy among cryptococcal antigen– positive people to prevent the development of invasive cryptococcal disease are recommended before initiating or reinitiating ART for PLHIV who have a CD4 count.<100 cells/mm3” (strong recommendation, moderate certainty evidence).[1]

Ford et al’s systematic review showed that Africa had the highest prevalence of CD4<100 cells/mm3 and the authors suggest that “consideration should be given to screening at a higher CD4 count of <200 cells/mm3 in settings where there are sufficient resources to implement such an approach, or where a simplified package of care for advanced disease is required based on a unified CD4 threshold”.[2]

The South African HIV Clinician Society Guideline[3] recommends reflex monitoring of CrAg at a CD4 ≤200 cells/mm3. A NHLS technical report, based on a period where the CD4 threshold for CrAg testing was temporarily increased from 100 to 200 cells/mm3 found that there was an increase of 36% in detected cryptococcal antigenaemia, with a prevalence of 2.6% in the 100-200 cell/mm3 range which exceeded the previously-determined 0.6% threshold cut-off for cost-effectiveness.

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[1] WHO. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach, July 2021.
[2] Ford N, Shubber Z, Jarvis JN, Chiller T, Greene G, Migone C, Vitoria M, Doherty M, Meintjes G. CD4 Cell Count Threshold for Cryptococcal Antigen Screening of HIVInfected Individuals: A Systematic Review and Meta-analysis. Clin Infect Dis. 2018 Mar 4;66(suppl_2):S152-S159.
[3] Nel J, Meintjies G, Osih R et al. Southern African HIV Clinicians Society guidelines for antiretroviral therapy in adults: 2023 update.

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Monitoring on ART: Cryptococcal Antigen (CrAg) Screening

NEMLC Recommendation

Following engagement with both the NHLS and the National HIV program guideline team, the **NEMLC recommends** that a threshold of CD4 ≤200 cells/mm^3 be applied, in view of the clinical value, and given that state facilities currently offer reflex testing at less than 100 cells/mm^3

STG Amendments: AHL Chapter 10

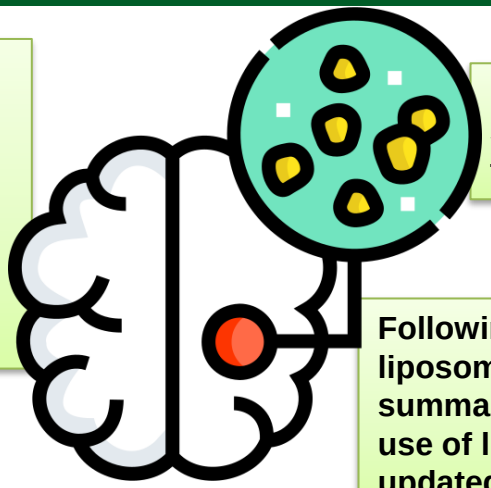
MONITORING ON ART

Baseline evaluation

- Confirm HIV positive result with second test.
- WHO staging.
- Check CD4 count.
- If CD4 <200 cells/mm^3:
  - Check cryptococcal antigen (if positive, perform LP regardless of whether symptoms are present or not).
  - Initiate cotrimoxazole prophylaxis (See Section 10.2.2: Cotrimoxazole prophylaxis).
  - Reflex CrAg testing is done on the CD4 sample if CD4 <100 cells/mm^3. If patient's CD4 is 100-199, a serum CrAg test must be ordered separately.

Cryptococcosis

NEMLC had previously recommended that flucytosine be considered for inclusion in the EML, once SAHPRA registered and if the price for the oral regimen was reduced by 42% (R2195 per pack of 500mg, 100 tablets).



Flucytosine was registered by SAHPRA in December 2021 and the STG has been updated.

Following a reduction in the price of liposomal amphotericin B, the evidence summary and associated cost analysis for the use of liposomal amphotericin B was updated.

Algorithm for the prevention, diagnosis and management of cryptococcosis among PLHIV: *Amended* ART (if CSF CrAg negative*): Directions for use amended (timing of initiation)*

Treatment algorithm was amended for clarity purposes and correctness. It was noted that NEMLC had previously recommended that the SA HIV Clinicians Society algorithm be adapted, and the option to refuse a lumbar puncture be removed from the algorithm. Therefore, this section was delineated into management for

i) CSF CrAg negative and

ii) Cryptococcal meningitis, aligned with the most recent SA HIV Clinician Society algorithm.

Additionally, the algorithm also includes guidance for the use of a liposomal amphotericin regimen in combination with flucytosine

Perform serum CrAg test when CD4 <200 cells/mm³

- **POSITIVE** → **Lumbar puncture (LP)**
  - **CSF +ve for CrAG** → **INDUCTION PHASE**
    - **Liposomal amphotericin B and flucytosine available:**
      Liposomal amphotericin B, IV infusion over 2hrs, 10mg/kg, as a single dose.
      AND
      Flucytosine, oral, 25mg/kg every 6hrs for 14 days.
      AND
      Fluconazole, oral , 1200mg daily for 14 days.
    - **Liposomal amphotericin B is not available :**
      Amphotericin B deoxycholate, IV infusion over 4hrs, 1mg/kg daily for 7 days.
      AND
      Flucytosine, oral 25mg/kg every 6hrs for 7 days.
      THEN
      Fluconazole, oral 1200mg daily for 7 days.
      AND
      Flucytosine, oral 25mg/kg every 6hrs for 7 days *(i.e. total 14 days).*
    - **Flucytosine is not available:**
      Fluconazole, oral 1200 mg daily for 14 days.
      AND
      Amphotericin B deoxycholate, IV infusion over 4hrs, 1mg/kg daily for 14 days.

    → **CONSOLIDATION PHASE**
    Fluconazole, oral, 800 mg daily for 8 weeks.
- **NEGATIVE**
  CSF -ve for CrAG
  Start ART
  Screen for other OIs
  → **INDUCTION PHASE**
  Fluconazole, oral 1200 mg daily for 14 days.
  → **CONSOLIDATION PHASE**
  Fluconazole, oral, 800 mg daily for 8 weeks.

→ **MAINTENANCE PHASE**
Fluconazole, oral, 200 mg daily.
Continue for at least 1 year provided that the CD4 count increases to >200 cells/mm³ on ART. If the CD4 count does not increase continue treatment indefinitely.

If there is a delay in performing LP, obtaining LP results or in starting amphotericin therapy, start fluconazole 1200mg immediately.

Post-Exposure Prophylaxis (PEP): Notable Amendments

PEP for healthcare workers following hepatitis B exposure

Hepatitis B Immunoglobulin: *Amended*

Aligned with the National Clinical Guidelines of post-exposure prophylaxis (PEP) in occupational and non-occupational exposures

	Source patient			
	Vaccination status	**HBsAg positive**	**HbsAg negative**	**HBsAg unknown**
Vaccination status and antibody response status of HCW	Unvaccinated or vaccination incomplete	• HBIG, IM, 500 units* • Hep B vaccine (3 doses at monthly intervals)	• Initiate Hep B vaccination (month 0, 1 and 6)	• HBIG, IM, 500 units* • Hep B vaccine (3 doses at monthly intervals)
	Vaccinated **AND** known to have HBsAb ≥10 units/mL#	No treatment	No treatment	No treatment
	Vaccinated **AND** HBsAb <10 units/mL or level unknown	• HBIG, IM, 500 units * • If HBIG <10 units/mL, repeat HBIG at 1 month • Repeat Hep B vaccine (3 doses at monthly intervals)	No treatment	• HBIG, IM, 500 units* • If HBIG <10 units/mL, repeat HBIG at 1 month • Repeat Hep B vaccine (3 doses at monthly intervals)

Delay in obtaining HBsAb results

Time period of delay: *Amended*

Aligned with the National Clinical Guidelines of post-exposure prophylaxis (PEP) in occupational and non-occupational exposures

If the delay in obtaining HBsAb results is more than ~~24 hours~~ 7 days initiate treatment as for vaccinated AND HBsAb < 10 units/mL.

Non-occupational PEP, Sexual Assault:

Emergency contraception Copper IUCD: *Added (as first line option)*

Levonorgestrel, oral: *Retained (as 2nd line option)*

Copper IUCD placed as the first line option as this agent has less drug-drug interactions compared to oral levonorgestrel 1.5mg and is the agent of choice for obese women. Copper IUCD can also be used as a long-acting reversible contraceptive.

Thank You!!